

CLAIMS

We claim:

- 1. A targeting construct comprising:
 - (a) a first polynucleotide sequence homologous to a NOR1 gene;
 - (b) a second polynucleotide sequence homologous to the NOR1 gene; and
 - (c) a selectable marker.
- 2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
- 3. A method of producing a targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to a NOR1 gene;
 - (b) providing a second polynucleotide sequence homologous to the NOR1;
 - (c) providing a selectable marker; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
- 4. A method of producing a targeting construct, the method comprising:
 - (a) providing a polynucleotide comprising a first sequence homologous to a first region of the NOR1 gene and a second sequence homologous to the NOR1 gene; and
 - (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.
- 5. A cell comprising a disruption in a NOR1 gene.
- The cell of claim 5 wherein the cell is a murine cell.
 - The cell of claim ϕ , wherein the murine cell is an embryonic stem cell.
- 8. A non-human transgenic animal comprising a disruption in a NOR1 gene.
- 9. A cell derived from the non-human transgenic animal of claim 8.
- 10. A method of producing a transgenic mouse comprising a disruption in the NOR1 gene, the method comprising:
 - (a) introducing the targeting construct of claim 1 into a cell;
 - (b) introducing the cell into a blastocyst;
 - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

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- (d) breeding the chimeric mouse to produce the transgenic mouse.
- 11. A method of identifying an agent that modulates the expression or function of NOR1, the method comprising:
 - (a) providing a non-human transgenic animal comprising a disruption in a NOR1 gene;
 - (b) administering an agent to the non-human transgenic animal; and
 - (c) determining whether the expression or function of NOR1 in the non-human transgenic animal is modulated.
- 12. A method of identifying an agent that modulates the expression or function of NOR1, the method comprising:
 - (a) providing a cell comprising a disruption in a NOR1 gene;
 - (b) contacting the cell with an agent; and
 - (c) determining whether expression or function of NOR1 is modulated.
- 13. An agent identified by the method of claim 11 and claim 12.
- The non-human transgenic animal of claim 8, wherein the transgenic animal exhibits increased or enhanced pain response threshold.
- 16. The non-luman transgenic animal of claim 8, wherein the transgenic animal exhibits impaired balance and impaired motor coordination.
- 16. A method of identifying an agent that ameliorates impaired balance and motor coordination, the method comprising administering an agent to the non-human transgenic animal of claim 15 and determining whether the agent ameliorates impaired balance and motor coordination.
- 17. A method of identifying an agent that improves balance and motor coordination, the method comprising administering an agent to the non-human transgenic animal of claim 15 and determining whether the agent ameliorates impaired balance and motor coordination.
- A transgenic mouse comprising a disruption in a NOR1 gene, wherein the transgenic mouse exhibits increased or enhanced pain response threshold.
- 19. A transgenic mouse comprising a disruption in a NOR1 gene, wherein the transgenic mouse exhibits impaired balance and impaired motor coordination.
- 20. A method of identifying an agent that affects a phenotype associated with a disruption in a NOR1 gene, the method comprising:
 - (a) providing a transgenic mouse comprising a disruption in a NOR1 gene;

- (b) administering an agent to the transgenic mouse; and
- (c) determining whether agent affects a phenotype in the non-human transgenic animal, wherein the phenotype is increased or enhanced pain response threshold or impaired balance and impaired motor coordination.
- 21. A method of identifying an agent that modulates the expression or function of NOR1, the method comprising:
 - (a) providing a transgenic mouse comprising a disruption in a NOR1 gene;
 - (b) administering an agent to the transgenic mouse; and
 - (c) determining whether agent modulates the expression or function; wherein the agent modulates enhanced pain response threshold or impaired balance and impaired motor coordination.
- 22. A method of identifying a compound that inhibits the activity of NOR1, the method comprising:
 - (a) providing a cell expressing NOR1;
 - (b) contacting the cell with a test compound; and
 - (c) determining whether the activity of NOR1 is decreased in the presence of the compound.
- 23. An agent identified by the method of claim 16, claim 17, claim 20, claim 21, or claim 22.
- 24. A method of ameliorating impaired balance or impaired motor coordination, the method comprising administering to a subject in need a therapeutically effective amount of NOR1.
- 25. A method of improving balance and motor coordination, the method comprising administering to a subject in need a therapeutically effective amount of NOR1.
- 26. A pharmaceutical composition comprising NOR1.